California Cancer Commission Studies* Chapter XI

Cancer of the Lip

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FAILURE to reduce the mortality in carcinoma of the lip to near zero is well-nigh inexcusable. The great majority of these lesions develop slowly through well recognizable precancerous states over a considerable period of time. They are invariably on the exposed mucosa of the lips, usually in full view of the patient and readily accessible to simple biopsy for accurate diagnosis. Lesions arising on the skin of the lip should not be confused with these, for they behave as skin cancers elsewhere and should be so treated. In most instances carcinoma of the lip is relatively slow in its local growth and usually dilatory in its spread to immediately adjacent regional lymph nodes. The failure to cure cancer of the lip is the direct responsibility of the patient who does not seek treatment soon enough, or of the physician who neglects proper measures for prompt diagnosis and immediate, radical treatment.

Cancer is the first diagnostic possibility to be considered in any lesion of the lips, particularly in males past middle age. The physician also has an important function in the prevention of this form of cancer through proper treatment of precancerous lesions.

PRECANCEROUS LESIONS

The term "precancerous" implies the possibility and not the inevitability of malignant growth. Approximately 50 per cent of cancer of the lip arises in such lesions.

*Organized by the Editorial Committee of the California Cancer Commission.

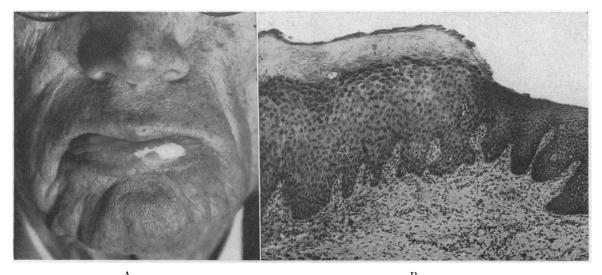
A. Leukoplakia and Keratoses. These two processes represent the most common precursors of cancer of the lip. Inasmuch as they resemble one another in their etiology, histopathology, progress and management, they may conveniently be considered together.

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- 1. Etiology. Chronic irritation is the most important factor. This may come from repeated exposure to the sun and wind, chemical and thermal irritants and repeated trauma, such as mucosal tears from cigarette paper. Vitamin deficiencies may also be of importance.
- 2. Clinical Appearance. Leukoplakia varies from areas of pallor or greyish white film over the mucosa (Figure 1) to localized single or multiple diffuse white or faintly bluish plaques which are soft to firm, flat or slightly elevated. (Figure 2.)

Keratoses may be single, multiple (Figure 3) or involve the lip diffusely; the latter occurs more commonly in younger individuals. In older persons areas of alternate crusting and scaling eventually lead to erosion and a chronic inflammatory exudate in the submucosa. Thick crusts of keratotic epithelium may elevate such lesions above the adjacent mucosa. Repeated exfoliation with slight bleeding is a frequent signal of early carcinoma developing in the base of the lesion.

3. Treatment. Any distinct induration, erosion or ulceration in leukoplakia or keratosis demands immediate biopsy. Superficial lesions, small in area, are well treated by electrocoagulation, actual caut-



A B

Figure 1.—(a) Leukoplakia. (b) Photomicrograph of (a) showing abrupt border of dense keratotic surface, hyperplasia of underlying squamous cells.



Figure 2.—Diffuse keratosis with erosion and secondary infection. Illustrates difficulty in differentiation from carcinoma.

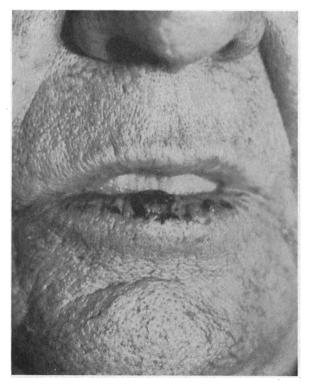


Figure 3.—Multiple localized areas of keratosis. Central lesion resembles papillary carcinoma.

ery, or excision. The latter offers the dual advantage of being diagnostic and curative, and in older individuals confirms the benign character of this classical precancerous process. Diffuse states of leukoplakia can be treated by brush cautery or wide mucosal excision and cheiloplasty. Leukoplakia which has become fissured, piled up or indurated should be completely excised. This can be done by elliptical incisions parallel to the vermillion border and undercutting the mucosa to secure closure. Filmy leukoplakia should be carefully watched. These processes do not respond to irradiation.

4. Preventive Measures. The patient who has developed leukoplakia or keratoses after definitive treatment of distinct lesions should employ measures aimed at prevention of further abnormal changes. Young individuals with diffuse, very superficial changes usually respond well to daily use of boric acid or plain lanolin ointment. Patients should carry with them a tube of white pommade and apply it several times daily to the lips. Large doses of B-complex vitamins, preferably in the form of brewer's yeast, may be helpful. Some individuals acutely sensitive to actinic radiation may be forced to a change of occupation to avoid sunshine. The use of tobacco should be discontinued or cut to the minimum. Oral hygiene should be scrupulous.

B. Cheilitis, Fissures and Ulcers. Diffuse inflammation, usually of the lower lip, is most common in young individuals with actinic intolerance. (Figure 4.) In advanced nutritional deficiencies the process may involve the commissures (perleche). Treatment consists in removal of causative factors and correction of nutritional deficiencies.

GRANULOMAS

A. Pyogenic Granuloma (Figure 5). Pyogenic granuloma is a chronic inflammatory proliferative process secondary to local non-specific infection. Trauma is usually recognized as the initiating factor, frequently by teeth or food particles. It appears as an elevated, round or ovoid, reddish tumor which is soft in its early stages; the surface has a "raspberry" appearance. Ölder lesions regress spontaneously, become fibrotic or become the site of warty, papillary excrescence. Histological examination shows characteristic form of highly vascular, organizing granulation tissue. The treatment of pyogenic granuloma, once the diagnosis is definitely established by biopsy, is local destruction by escharotic electrocoagulation or light doses of low voltage roentgen therapy.

B. Tuberculosis. This is a rare lesion of the lip, occurring near the vermillion border, nearly always associated with cavitating pulmonary and frequently oral tuberculosis. It appears as a punched out, soft ulcer, frequently with a greyish base. It is usually quite painful. Biopsy is the only dependable method of diagnosis.

C. Syphilis. The lip is an occasional site of a primary luetic lesion. The appearance of a well circum-

scribed, elevated denuded lesion with moderate induration suggests cancer. However, in the case of luetic lesion, its short duration, concommitant acute lymphadenopathy, positive darkfield and later positive Wassermann will establish the diagnosis.

RETENTION CYSTS (MUCOUS CYST, SIMPLE CYST)

These cysts are due to occlusion of a mucous gland duct, secondary to inflammation or trauma. They are dome shaped, bulging, translucent bluish swellings, usually on the buccal surface of either lip. They

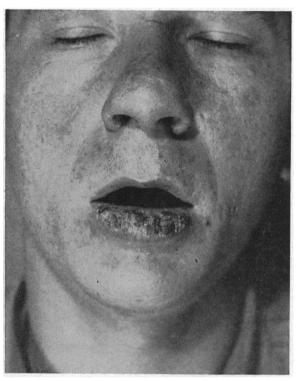


Figure 4.—Diffuse cheilitis in young individual.

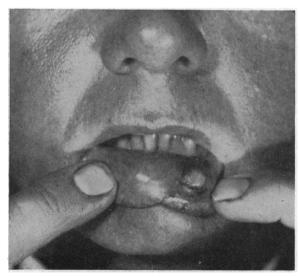


Figure 5.—Pyogenic granuloma.

are fluctuant unless under extreme pressure of contained secretion. Treatment consists in local excision with entire removal of the capsule.

BENIGN NEOPLASMS

Benign neoplasms may be of epithelial or, less commonly, of mesodermal origin.

A. Squamous Papilloma. These are soft, papillary or warty excrescences sometimes occurring around the commissures. Squamous carcinoma may arise in such originally benign lesions. The danger signals are increased growth, induration or ulceration. The treatment is adequate local excision with a margin of normal tissue.

B. Hemangioma. Lymphangioma.

1. Congenital

a. The familiar "birth mark" of infants frequently involves the stomal structures with submucosal extension into the lips. Both the simplex and cavernous types of hemangioma are seen. Superficial lesions respond to minute doses of surface irradiation, carbon dioxide snow, or electro-desiccation. The deeper and cavernous tumors are best treated primarily with external irradiation, insertion of weak radon gold seeds, injection of sclerosing solutions, and surgical excision of the residual tumor if required with appropriate cheiloplasty.

b. Lymphangiomas (cystic hygroma) produce some degree of the condition referred to as macrocheilia, a diffuse soft, spongy enlargement of the lip, usually without mucosal involvement. Irradiation is ineffective, and surgical measures are indicated.

c. Mixed hemangioma lymphangioma occurs rarely. The response to irradiation will be in proportion to the amount of angiomatous elements present.

2. Acquired Angioma, involving the lips in adults are usually the result of trauma. They constitute smooth, bluish to reddish, soft swellings. Surgical excision is required.

C. Mixed Salivary Gland Tumors. Five per cent of these tumors originate in accessory salivary glands, and of these, rare examples are seen in the lips. Their structure and potentially malignant characteristics are identical with their more usual counterpart in the parotid gland.

D. Melanoma of peri-stomal location usually has its origin in the adjacent skin, but there are rare examples of a primary melanoma of the lip. They show the characteristic brown to blue-black pigmentation, and require differentiation from the hemangiomas. Immediate wide excision is required.

SQUAMOUS CARCINOMA (EPIDERMOID, PRICKLE CELL CARCINOMA)

A. Definition. Squamous-cell cancer is a malignant neoplasm arising in the mucosa of the lips and is capable of metastasizing to regional cervical lymph nodes. Squamous carcinoma of the lip proper must be differentiated from malignant neoplasms arising

in adjacent sites, which may invade the lip secondarily, such as basal cell carcinoma of the skin, melanoma, carcinoma of the alveolus.

- B. Etiology. Squamous carcinoma arises almost uniformly on a basis of chronic traumatism, frequently in an already profoundly altered tissue bed provided by the "precancerous" factors in the individual's tissue reacting to unfavorable environmental stimuli. Yet many individuals exhibiting such stigmata do not develop cancer, while in others cancer of the lip may occasionally arise in apparently healthy epithelium.
- C. Incidence. The lower lip is the primary site in 96 per cent, the commissures and upper lip in 4 per cent. Occupational exposure makes it a cancer largely seen in males, 80 per cent. Predominantly it is a disease of late middle life and old age, although a few cases occur in young adults.
- D. Clinical Types. As in many forms of cancer, the gross morphology of the tumor is a reasonably reliable clue to its pattern of growth and degree of malignancy.
- 1. Papillary, Extrovertive Type. In its earliest stage this type is seen as a thickened, slightly elevated, indurated plaque in the mucosa proper, or as a warty lesion which crusts and scales superficially. (Figure 6.) Its progress is that of peripheral growth, with a gradual advance of its border in the direction of the commissure. It may become considerably elevated and form a protruding verrucous mass. The spread of this type toward the muscularis is dilatory, and it is usually late in its metastases to the regional nodes. Eventually it ulcerates, undergoes necrosis, and pursues the course of an infiltrating carcinoma.
- 2. Ulcerative, Infiltrating Type (Figure 7 and 8). This form may begin as a flat plaque which ulcerates early and is destructive from the beginning, or it may be seen first as a submucosal nodule with smooth overlying mucosa, to which it is attached. An ulcer is soon produced which exhibits loss of substance of the lip. This tumor soon infiltrates the muscularis. Secondary infection may be severe, with cellulitis and edema of the adjacent chin and regional lymphadenitis.
- E. Metastases. Generally carcinoma of the lip is late to metastasize to the cervical nodes, the exceptions being provided by the more malignant deeply ulcerating types. Many cases are seen of six to twelve months' duration without palpable regional nodes. Cancer of the lip almost uniformly pursues a regular anatomical pattern of lymphatic spread. The nodes involved, in order of succession, are usually: submaxillary or submental, superior cervical (carotid), lower cervical, and supraclavicular.
- F. Histopathology. The microscopic appearance varies greatly, from well differentiated squamous carcinoma to a purely anaplastic type. The majority are well differentiated.
- G. Treatment. Cancer of the lip is a lethal disease.

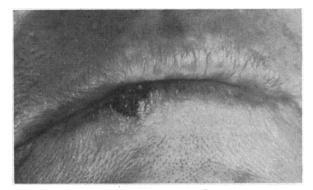


Figure 6.—Early papillary form of carcinoma.

Courtesy of Dr. George Sharp.



Figure 7.—Early ulcerative form of carcinoma.

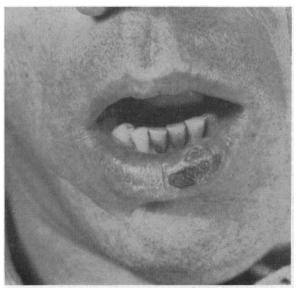


Figure 8.—Ulcerative carcinoma in a 19 year old man.

Any lesion of the lip that persists more than four weeks should be considered as cancer until a biopsy is taken. Proven cancer of the lip requires radical treatment by surgery or irradiation. The first treatment should be the last. While 90 per cent of uncomplicated, previously untreated lip cancer is curable, only 40 to 60 per cent of recurrent lip cancer can be cured.

The treatment of lip cancer requires total destruction, or complete, radical removal of all neoplastic cells by whatever method is employed. It requires control of the primary tumor and evaluation of possible lymph node involvement and treatment thereof. Although the best possible cosmetic result will be sought, this issue should be recognized as entirely subordinate to the more urgent problem of cure. Inadequate treatment is worse than none at all.

- 1. Treatment of Primary Tumor.
- a. Lesions up to 2 cm. in greatest diameter, with extension not more than half-way toward the cheilogingival groove.

This group includes lesions ranging from early, superficial to moderately advanced, or the majority of cases seen in ordinary practice. For these lip cancers (Figures 9 and 10), cancericidal doses of x-ray or radium and surgical excision are equally effective and produce the same cure rate. Many radiologists contend that better cosmetic results are obtained by irradiation. V-excisions must be full thickness resections which go far wide of the tumor, and the margins should be examined for microscopic verification of the surgeon's judgment. With irradiation, for tumors invading the lip for a depth of 1 cm. or more, surface irradiation needs supplemental interstitial radium.

b. Lesions deeply infiltrating toward or involving the cheilo-gingival groove.

These advanced tumors are unsuitable for irradiation methods. Radical surgery is required. X-ray films to rule out involvement of the mandible are necessary; and even if the latter be present, cure may still be achieved in favorable cases with resection of the mandible.

Radical surgical treatment of these advanced cases implies a measure of skill and special experience, and a willingness to undertake an arduous, time-consuming and mutilating procedure. It involves removal of most of or all the lower lip and chin, wide mobilization of skin and mucosal flaps from the face and neck and buccal surfaces respectively, with immediate plastic reconstruction of a new lower lip.

- c. Recurrent carcinoma of the lip, postoperative or postirradiation, is best treated by radical surgery.
- 2. Treatment of Regional Lymph Nodes. The primary consideration is to determine whether there is clinical evidence suggestive of regional nodal metastases. Some ulcerated carcinomas of the lip exhibit a regional lymphadenitis which regresses after control and healing of the primary site. For this reason, it is best to delay final decision on the regional nodes until six weeks after treatment of the primary tumor. At this time the patient's status may be evaluated according to the following criteria, providing the lip lesion is controlled:
- a. No submental or submaxillary lymphadenopathy can be determined:*

^{*}It should be remembered that a few small (0.5 to 1.0 cm.) soft to even moderately firm nodes may normally be palpated in the neck.



Figure 9.—Ulcerative carcinoma before and after treatment by irradiation.



Figure 10.—Diffuse papillary carcinoma before and after treatment by irradiation.

Only one out of ten such patients will subsequently develop metastases. To perform routine "prophylactic" block dissections on such patients would then be equivalent to doing nine unnecessary procedures for the benefit of one patient who can be almost as effectively treated by prompt action when his nodes do appear. Prophylactic neck dissections in cancer of the lip are therefore not recommended. So-called prophylactic irradiation of neck nodes is of no value and should be condemned.

b. Six weeks after treatment, regional nodes suggestive of metastases are present:

In such cases immediate block dissection is required. Usually a suprahyoid neck dissection is adequate, cleaning out both submental and submaxillary triangles and removing both submaxillary salivary glands. In occasional lesions located lateral to the midline in which a carotid node seems involved, a block dissection of the entire side of the neck is indicated. Some surgeons do a complete neck dissection if the submaxillary triangle is involved. Radiation therapy has no place in curative treatment of metastases in cervical nodes, for here the neoplasm develops a radioresistant status that makes such treatment palliative rather than curative.

3. Palliative Treatment. Incurable primary or metastatic disease is treated for palliation by radiation therapy.

PROGNOSIS

The cure rate in carcinoma of the lip is higher than for any other form of oral cancer. Permanent cure of the primary tumor is achieved in 90 per cent of consecutive cases. By modern procedures about 80 per cent of patients will be free of disease after five years, including those treated for regional metastases. In the group having metastases the five-year cure rate will be 25 to 30 per cent.

NOTE BY EDITORIAL COMMITTEE

When the California Medical Association published its cancer studies in 1936 there was wide divergence of opinion regarding the treatment of the nodal area in cancer of the lip. Such divergence still exists. Many surgeons advise routine bilateral suprahyoid dissections in all cases. At the other extreme are those who advise node dissection only in the presence of proven operable metastasis.

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No one can take issue with the necessity for the procedure when metastasis is proven and operable. The question of dissection in all cases is not so easily settled. Neither palpability nor enlargement, in itself, signifies metastasis. Normal nodes are frequently palpable; enlargement may be due to inflammation. Impalpability, on the other hand, does not signify absence of metastases in all cases. However, the percentage of unexpected involved nodes, in various published series of routine dissections ("prophylactic") is so small as to gainsay that course when one considers the high percentage of operations performed unnecessarily. It appears even less warranted when one recognizes that in some reported series the operative mortality approaches closely the percentage of cases in which metastatic nodes are found and presumably benefited. In some series the operative mortality is even greater.

The Editorial Committee believes that routine dissection

The Editorial Committee believes that routine dissection is contraindicated, that somewhere between the two extremes is the course to be followed as determined by the merits of the individual patient.

If surgical treatment is contraindicated, cervical metastasis may be cured in some cases by a proper use of combined external and interstitial irradiation. All is not lost because a patient cannot stand operation or has a recurrence in the neck following dissection.

Chapter XIII of the California Cancer Commission Studies "Cancer of the Tonsil and Pharynx," by Lewis F. Morrison, M.D., will appear in this section in the February issue of California Medicine.